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DC 20231

Ruth Montalvo

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:

Yoshihiko MAKINO, et al.

Group: 1655

Serial No.:

09/802,232

Examiner: F.W.M LU

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METHOD FOR TESTING COMPLEMENTATION OF NUCLEIC ACID

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Commissioner for Patents Washington, D. C. 20231

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## **RESPONSE**

Sir:

This is in response to the Office Action mailed July 26, 2002, please amend the above identified application as follows:

## IN THE CLAIMS

1. (amended) A method for testing complementation of nucleic acid fragment which comprises the steps of:

bringing a sample nucleic acid complex which comprises a double-stranded nucleic acid structure and a labeled intercalator intercalated therein, in which the double-stranded nucleic acid structure has been produced by contact of a sample nucleic acid fragment with a probe molecule fixed to a solid carrier in the presence of an aqueous medium, the sample nucleic acid fragment being partly complementary to the probe molecule, the probe molecule being selected from the group consisting of a nucleic acid or a nucleic acid derivative, into contact with an aqueous medium;

applying variation of a physical or chemical surrounding conditions to the

latter aqueous medium, to cause disengagement of the sample nucleic acid fragment and the intercalator from the nucleic acid complex and simultaneously measuring decrease of quantity of the label on the solid carrier, so that stability of the sample nucleic acid fragment of the complex is determined; and

comparing the stability determined above with reference stability data which are separately obtained by determination of stability of a reference nucleic acid fragment in a reference nucleic acid complex comprising a reference double-stranded nucleic acid structure and the labeled intercalator intercalated therein in which the reference double-stranded nucleic acid structure is produced by contact of the reference nucleic acid fragment with the probe molecule, the reference nucleic acid fragment being determined in complementation thereof with the probe molecule.

11. (amended) A method for testing complementation of nucleic acid fragment which comprises the steps of:

bringing a sample nucleic acid fragment into contact with a probe molecule fixed to a solid carrier in the presence of an aqueous medium and a labeled intercalator to produce on the solid carrier a sample nucleic acid complex comprising a double-stranded nucleic acid structure and the labeled intercalator intercalated therein, the sample nucleic acid fragment being partly complementary to the probe molecule, the probe molecule being selected from the group consisting of a nucleic acid or a nucleic acid derivative, while applying variation of physical or chemical surrounding conditions to the aqueous medium, so that stability of the sample nucleic acid fragment in the complex is determined; and

comparing the stability determined above with reference stability data which are separately obtained by determination of stability of a reference nucleic acid fragment in a reference nucleic acid complex comprising a reference double-stranded nucleic acid structure and the labeled intercalator intercalated therein in which the reference double-stranded nucleic acid structure is produced by contact of the reference nucleic acid

fragment with the probe molecule, the reference nucleic acid fragment being determined in complementation thereof with the probe molecule.

## **REMARKS**

As a result of the foregoing amendment, independent claims 1 and 11 have been amended to recite that the sample nucleic acid fragment is partly complementary to the probe molecule. This is in accordance with the original disclosure at page 3, line 34 to page 4, line 2.

As was pointed out in the last filed response the disclosure of the Piunno et al reference differs significantly from the presently claimed invention and does not provide a proper basis for rejection either under 35 USC 102 or 35 USC 103. In particular, Piunno et al contains no information with respect to the differentiation between the fully complementary relationship to form a full match structure and the partly complementary relationship to form the mismatched structure. The examiner noted in the office action at page 9 that the claims did not require such differentiation. However, as a result of the foregoing amendment, this limitation has been placed into the claims. Accordingly, this argument is fully supported by the claims as amended and fully differentiates the presently claimed invention from the Piunno et al disclosure. Consequently, the rejection of the claims as being anticipated or rendered obvious by this reference has been obviated and should be withdrawn.

The remaining claims i.e., claims 4, 5, 6, 14, 15 and 16 which were rejected as being obvious over the Piunno et al reference, in as much as they are dependent from either claims 1 or 11, are also now allowable over this reference. Again, Piunno et al fails to teach anything concerning the limitation now in the claims regarding the fact that the sample nucleic acid fragment is partly complementary to the probe molecule. Accordingly, all of these rejections are untenable and should be withdrawn.

Entry of the foregoing amendment is requested in as much as it clearly places the application in condition for allowance at this time and favorable reconsideration and prompt notice to that effect are earnestly solicited.

Respectfully submitted,

December 26, 2002

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